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TO: Ralph J Gitomer
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Thursday, October 19, 2006

Case Serial Number: 10/039952

From: Noble Jarrell
Location: Biotech-Chem Library
Rem 1B71
Phone: 272-2556

Noble.jarrell@uspto.gov

Search Notes

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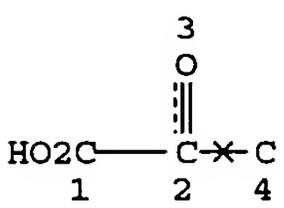


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DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   4

STEREO ATTRIBUTES: NONE
L13         9467 SEA FILE=REGISTRY SSS FUL L11

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FILE COVERS 1907 - 19 Oct 2006 VOL 145 ISS 17
FILE LAST UPDATED: 18 Oct 2006 (20061018/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitind hitstr retable l28 tot

L28 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:353585 HCAPLUS
DN 136:352318
TI Method for chemical transformation using a mutated enzyme
IN **Rozzell, J. David, Jr.**
PA **Biocatalytics, Inc., USA**
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2002036742	A2	20020510	2001WO-US48577	20011030 <--
	WO2002036742	A3	20030821		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US2002061564	A1	20020523	2001US-0039952	20011024 <--
	AU2002032603	A5	20020515	2002AU-0032603	20011030 <--
PRAI	2000US-0702421	A	20001031	<--	
	2001US-288378P	P	20010503	<--	
	2001US-0039952	A	20011024	<--	
	2001WO-US48577	W	20011030		

AB The invention concerns methods for chemical transforming compds. using a mutated enzyme are provided, and more particularly a method for the production of an amino acid from a target 2-ketoacid, the production of an amine from a target ketone and the production of an alc. from a target ketone. The methods comprise creating a mutated enzyme that catalyzes the reductive amination or transamination of the target 2-ketoacid or ketone or the reduction of the ketone and providing the mutated enzyme in a reaction mixture comprising the target 2-ketoacid or ketone under conditions sufficient to permit the formation of the desired amino acid, amine or alc. to thereby produce the amino acid, amine or alc.

IC ICM C12N
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 6, 7
IT Chirality
Indicators
Mutagenesis
Optical detectors
Oxidation
Reduction
Transamination
pH
(method for chemical transformation using a mutated enzyme)
IT **Enzymes, uses**

RL: CAT (Catalyst use); PRP (Properties); USES (Uses)
(method for chemical transformation using a mutated enzyme)

IT **Ketones, reactions**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); **RCT (Reactant)**; PROC (Process); **RACT (Reactant or reagent)**
(method for chemical transformation using a mutated enzyme)

IT Alcohols, preparation
Amines, preparation
Amino acids, preparation
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(method for chemical transformation using a mutated enzyme)

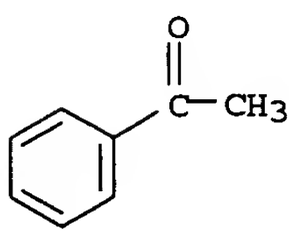
IT **Amination**
(reductive; method for chemical transformation using a mutated enzyme)

IT **98-86-2**, Acetophenone, reactions **99-91-2**, p-Chloroacetophenone 2142-63-4, m-Bromoacetophenone
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); **RCT (Reactant)**; PROC (Process); **RACT (Reactant or reagent)**
(method for chemical transformation using a mutated enzyme)

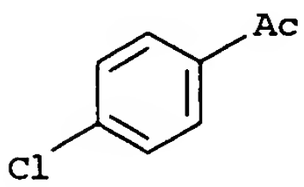
IT 70-11-1P, Bromoacetophenone 98-85-1P, 1-Phenylethanol 532-27-4P, Chloroacetophenone **618-36-0P**, 1-Phenylethylamine 2627-86-3P, S-1-Phenylethylamine 3886-69-9P 4187-56-8P, S-1-(p-Chlorophenyl)ethylamine 27298-99-3P 139305-96-7P 176707-77-0P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**; PROC (Process)
(method for chemical transformation using a mutated enzyme)

IT **98-86-2**, Acetophenone, reactions **99-91-2**, p-Chloroacetophenone
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); **RCT (Reactant)**; PROC (Process); **RACT (Reactant or reagent)**
(method for chemical transformation using a mutated enzyme)

RN 98-86-2 HCAPLUS
CN Ethanone, 1-phenyl- (9CI) (CA INDEX NAME)



RN 99-91-2 HCAPLUS
CN Ethanone, 1-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



IT **618-36-0P**, 1-Phenylethylamine
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**; PROC (Process)
(method for chemical transformation using a mutated enzyme)

RN 618-36-0 HCAPLUS
CN Benzenemethanamine, α-methyl- (9CI) (CA INDEX NAME)

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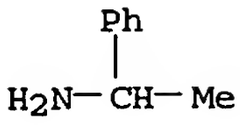
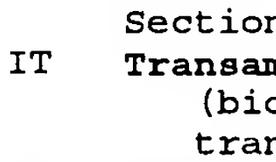
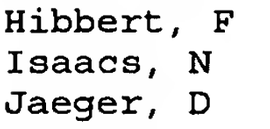


L28 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:335089 HCAPLUS
DN 137:93496
TI New Approach to Biomimetic Transamination Using Bifunctional [1,3]-Proton Transfer Catalysis in Thioxanthenyl Dioxide Imines
AU Hjelmencrantz, Anders; Berg, Ulf
CS Organic Chemistry 1, Department of Chemistry, Lund University, Lund, S-221 00, Swed.
SO Journal of Organic Chemistry (2002), 67(11), 3585-3594
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:93496
AB A pyridoxamine equivalent, 9-aminothioxanthene 10,10-dioxide, has been designed that is capable of affording transamination in good to excellent yields of natural as well as artificial amino acids. Amidines and guanidines in catalytic amts. were capable of performing [1,3]-proton transfer in the imines under mild conditions, whereas various simple amines failed. The use of chiral catalysts resulted in modest asym. induction (ee ≤ 45%). The electronic dependence in para-substituted Ph glyoxylate imines, isotope effects, and computational studies support a stepwise, bifunctional mechanism for amidine and guanidine catalysts. Attempts toward an autocatalytic model system are described.
CC 22-12 (Physical Organic Chemistry)
Section cross-reference(s): 7, 34, 67
IT **Transamination**
(biomimetic; biomimetic transamination using bifunctional [1,3]-proton transfer catalysis in thioxanthenyl dioxide imines)
IT **Amino acids, preparation**
RL: **PNU (Preparation, unclassified); PREP (Preparation)**
(esters; biomimetic transamination using bifunctional [1,3]-proton transfer catalysis in thioxanthenyl dioxide imines)
IT **Enzymes, uses**
RL: CAT (Catalyst use); USES (Uses)
(synthetic; biomimetic transamination using bifunctional [1,3]-proton transfer catalysis in thioxanthenyl dioxide imines)
IT **617-35-6**, Ethyl pyruvate **4170-30-3**, Crotonaldehyde **13192-04-6**, Dimethyl 2-oxoglutarate **15206-55-0**, Methyl benzoylformate **20201-24-5**, Ethyl 3-methyl-2-oxobutyrate **70091-75-7**, Ethyl p-nitrophenylglyoxylate
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(imination; biomimetic transamination using bifunctional [1,3]-proton transfer catalysis in thioxanthenyl dioxide imines)
IT **617-35-6**, Ethyl pyruvate **15206-55-0**, Methyl benzoylformate
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(imination; biomimetic transamination using bifunctional [1,3]-proton transfer catalysis in thioxanthenyl dioxide imines)
RN 617-35-6 HCAPLUS
CN Propanoic acid, 2-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 15206-55-0 HCAPLUS

CN Benzeneacetic acid, α-oxo-, methyl ester (9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Ahlberg, P	1989	2	429	J Phys Org Chem	HCAPLUS
Babudri, F	1996	52	13513	Tetrahedron	HCAPLUS
Beaulieu, F	1994	59	6508	J Org Chem	HCAPLUS
Berg, U	1997	51	778	Acta Chem Scand	HCAPLUS
Breslow, R	1990	112	5212	J Am Chem Soc	HCAPLUS
Cainelli, G	1996	61	5134	J Org Chem	HCAPLUS
Carpino, L	1989	54	5887	J Org Chem	HCAPLUS
Catscoulakos, P	1967	4	645	J Heterocycl Chem	
Chu, S	1975	B31	2134	Acta Crystallogr	HCAPLUS
Corey, E	1999	1	157	Org Lett	HCAPLUS
Dauwe, C	1995	2	171	Synthesis	
Dugas, H	1996			Bioorganic Chemistry	
Ek, M	1984	B38	211	Acta Chem Scand	HCAPLUS
Fasella, E	1999	7	709	Bioorg Med Chem	HCAPLUS
Guthrie, R	1971	93	5137	J Am Chem Soc	
Hehre, W				SPARTAN, version 5.0	
Hibbert, F	1983		1895	J Chem Soc, Perkin T	HCAPLUS
Isaacs, N	1995		152	Physical Organic Che	
Jaeger, D	1971	93	5153	J Am Chem Soc	HCAPLUS
Jaeger, D	1979	101	717	J Am Chem Soc	HCAPLUS
Janne, K	1976		1040	J Chem Soc, Chem Com	HCAPLUS
Kaempfen, U	1989	72	185	Helv Chim Acta	HCAPLUS
Lehninger, A	1993		511	Principles of Bioche	
Martell, A	1989	22	115	Acc Chem Res	HCAPLUS
Martell, A	1982	53	163	Adv Enzymol	HCAPLUS
Murphy, J	1995		1349	J Chem Soc, Perkin T	HCAPLUS
Panetta, C	1980	45	4503	J Org Chem	HCAPLUS
Roitenan, J	1971	90	2225	J Am Chem Soc	
Roitenan, J	1971	90	2231	J Am Chem Soc	
Soai, K	2000	33	382	Acc Chem Res	HCAPLUS
Soloshonok, V	1997	62	3030	J Org Chem	HCAPLUS
Soloshonok, V	1998	63	1878	J Org Chem	HCAPLUS
Soloshonok, V	1996	52	14701	Tetrahedron	HCAPLUS
Soloshonok, V	1996	52	6953	Tetrahedron	HCAPLUS
Su, W	1994	35	4955	Tetrahedron Lett	HCAPLUS
Taylor, D	1987	26	2167	Phytochemistry	HCAPLUS
Ternay, A	1974	39	2941	J Org Chem	
Toney, M	1993	32	1471	Biochemistry	HCAPLUS
Willems, J	1995	36	3917	Tetrahedron Lett	HCAPLUS
Wu, Y	1992	46	60	Acta Chem Scand	HCAPLUS
Wu, Y	1992	57	6324	J Org Chem	HCAPLUS

L28 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:501941 HCAPLUS
DN 135:331642
TI The development of new carboxylic acid-based MMP inhibitors derived from a cyclohexylglycine scaffold
AU Tullis, Joshua S.; Laufersweiler, Matthew J.; VanRens, John C.; Natchus, Michael G.; Bookland, Roger G.; Almstead, Neil G.; Pikul, Stanislaw; De, Biswanath; Hsieh, Lily C.; Janusz, Michael J.; Branch, Todd M.; Peng, Sean X.; Jin, Yingkun Y.; Hudlicky, Tomas; Oppong, Kofi
CS Health Care Research Center, Procter and Gamble Pharmaceuticals, Mason, OH, 45040, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(15), 1975-1979

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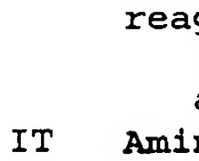
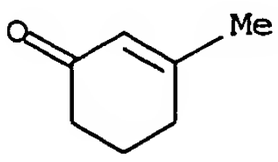
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 135:331642
AB A series of carboxylic acids was prepared based on cyclohexylglycine scaffolds and tested for potency as matrix metalloproteinase (MMP) inhibitors. Detailed SAR for the series is reported for five enzymes within the MMP family, and a number of inhibitors display low nanomolar potency for MMP-2 and MMP-13, while selectively sparing MMP-1 and MMP-7.
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7
IT **Enzyme** kinetics
(of inhibition; preparation and structure activity relationship of selective carboxylic acid-based MMP inhibitors using cyclohexylglycine scaffolds)
IT **Amino acids, preparation**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and structure activity relationship of selective carboxylic acid-based MMP inhibitors using cyclohexylglycine scaffolds)
IT **Amination**
(reductive; preparation and structure activity relationship of selective carboxylic acid-based MMP inhibitors using cyclohexylglycine scaffolds)
IT 62-53-3, Aniline, reactions 74-89-5, Methylamine, reactions 75-36-5, Acetyl chloride 100-46-9, Benzyl amine, reactions 107-21-1, Ethylene glycol, reactions 141-43-5, Ethanolamine, reactions 504-63-2, 1,3-Propane diol 628-12-6, 2-Methoxyethyl chloroformate **930-68-7**, 2-Cyclohexen-1-one 1013-88-3, Benzophenone imine **1193-18-6**, 3-Methyl-2-Cyclohexen-1-one 1667-04-5, Mesityl chloride 5680-79-5, Glycine, methyl ester, hydrochloride 22818-40-2 202752-04-3, 4'-Methoxy-4-biphenyl sulfonyl chloride
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(preparation and structure activity relationship of selective carboxylic acid-based MMP inhibitors using cyclohexylglycine scaffolds)
IT **930-68-7**, 2-Cyclohexen-1-one **1193-18-6**, 3-Methyl-2-Cyclohexen-1-one
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(preparation and structure activity relationship of selective carboxylic acid-based MMP inhibitors using cyclohexylglycine scaffolds)
RN 930-68-7 HCAPLUS
CN 2-Cyclohexen-1-one (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 1193-18-6 HCAPLUS
CN 2-Cyclohexen-1-one, 3-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Cheng, M	2000	43	369	J Med Chem	HCAPLUS

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Coker, M	1998	274	H1516	Am J Physiol	HCAPLUS
Corey, E	1998	39	5347	Tetrahedron Lett	HCAPLUS
Decrescenzo, G	1997			US-----12873	HCAPLUS
Decrescenzo, G	1997			US---9803166	
Hudlicky, T	2001	11	627	Bioorg Med Chem Lett	HCAPLUS
Kiyama, R	1999	42	1723	J Med Chem	HCAPLUS
Kiyama, R	1999	42	1723	J Med Chem	HCAPLUS
Leff, R	1999	878	201	Ann N Y Acad Sci	HCAPLUS
Lygo, B	1997	38	8595	Tetrahedron Lett	HCAPLUS
Natchus, M	2001	44	1060	J Med Chem	HCAPLUS
Nelson, A	2000	18	1135	J Clin Oncol	HCAPLUS
O'Brien, P	2000	43	156	J Med Chem	HCAPLUS
O'Brien, P	2000	43	156	J Med Chem	HCAPLUS
Parker, D	1997			WO---9722587	HCAPLUS
Pikul, S	2001			Bioorg Med Chem Lett	
Spinale, F	1999	85	364	Circ Res	HCAPLUS
Sugita, K	1999	1	475	Curr Opin Oncol, End	HCAPLUS
Tamura, Y	1998	41	640	J Med Chem	HCAPLUS
Whittaker, M	1999	99	2735	Chem Rev	HCAPLUS

L28 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:231355 HCAPLUS
DN 122:4971
TI Random chemistry for the generation of new compounds
IN Kauffman, Stuart A.; Rebek, Julius, Jr.
PA USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO---9424314	A1	19941027	1994WO-US04314	19940419
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA---2160457	AA	19941027	1994CA-2160457	19940419
AU---9468158	A1	19941108	1994AU-0068158	19940419
EP----695368	A1	19960207	1994EP-0916542	19940419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP--09500007	T2	19970107	1994JP-0523552	19940419
AU---9880020	A1	19981022	1998AU-0080020	19980814
US2005037435	A1	20050217	2004US-0933083	20040902
PRAI 1993US-0049268	A	19930419		
1994WO-US04314	W	19940419		
1996US-0537736	B1	19960129		
1997US-0882950	A1	19970626		

AB Methods for the generation of new compds. are disclosed. The present invention eliminates the need to know in advance the structure or chemical composition of a compound having a desired property. The disclosure of the present invention provides that diversity of unknown compds. may be produced by "random" chemical, and such a diversity of unknown compds. may be screened for one or more desired properties to detect the presence of suitable compds. In one aspect, a starting group of organic compds. is caused to undergo a series of chemical reactions to create a diversity of new organic compds. that are screened for the presence of organic compds. having the desired property. In another aspect of the present invention, a diversity of compds. is generated from a group of substrates which are subjected to group of enzymes representing a diversity of catalytic activities. The methodol. of the invention may be used to produce drugs, vaccines, etc. Preparation of ubiquitin fusion libraries with diversity of 1 x 107, as well as generation of a diversity of product mols., are described.

IC ICM C12Q-0001/68

ICS C12P-0019/34; C12P-0021/00; C12N-0015/63
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 21
IT Acylation
Addition reaction
Air
Alkylation
Amination
Carboxylation
Catalysts and Catalysis
Concentration condition
Condensation reaction
Deamination
Decarboxylation
Dehydration, chemical
Dehydrogenation
Dimerization
Elimination reaction
Epoxidation
Esterification
Halogenation
Hydrogenation
Hydrolysis
Isomerization
Nitration
Oxidation
Oxidizing agents
Pharmaceuticals
Pressure
Radiation
Reaction
Rearrangement
Reducing agents
Reduction
Ring cleavage
Ring closure and formation
Solvents
Substitution reaction
Sulfonation
Temperature
Transesterification
Vaccines
pH
(random chemical for the generation of new compds.)
IT **Enzymes**
RL: CAT (Catalyst use); USES (Uses)
(random chemical for the generation of new compds.)
IT **Amines, reactions**
RL: RCT (Reactant); RACT (Reactant or reagent)
(random chemical for the generation of new compds.)
IT **Ketones, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(random chemical for the generation of new compds.)

=> => b wpix
FILE 'WPIX' ENTERED AT 16:00:08 ON 19 OCT 2006

FILE LAST UPDATED: 18 OCT 2006 <20061018/UP>
MOST RECENT DERWENT UPDATE: 200667 <200667/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW AND ENHANCED DERWENT WORLD PATENTS INDEX TO BE RELEASED ON OCTOBER 22, 2006 <<<

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INDEX PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<


FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

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http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<
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>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS
INDEX PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

>>> NEW AND ENHANCED DERWENT WORLD PATENTS INDEX TO BE RELEASED ON
    OCTOBER 22, 2006 <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que sta l31
L11               STR
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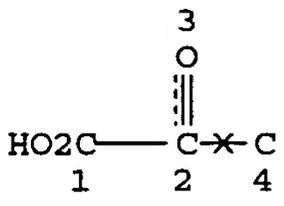


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   4

STEREO ATTRIBUTES: NONE
L31          509 SEA FILE=WPIX SSS FUL L11
100.0% PROCESSED   21622 ITERATIONS                    509 ANSWERS
SEARCH TIME: 00.00.07


=> d all abeq abex tech l62 tot

L62  ANSWER 1 OF 6  WPIX  COPYRIGHT 2006 THE THOMSON CORP on STN
AN   2005-050515 [06]   WPIX
DNN  N2005-044261       DNC C2005-017712
TI   Selecting optimal operating conditions for coupling reactions, useful e.g.
     in preparation of pharmaceuticals, particularly selection of catalysts,
     includes immunological detection of coupled products.
DC   B04 D16 E19 J04 S03
IN   CREMINON, C; RENARD, P Y; TARAN, F; RENARD, P
PA   (COMS) COMMISSARIAT ENERGIE ATOMIQUE
CYC  109
PI   FR-----2853965 A1 20041022 (200506)*      70    G01N-033-53
     WO--2004092729 A2 20041028 (200506)  FR         G01N-033-543
```

noble jarrell 19/10/2006

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW

EP-----1616185 A2 20060118 (200606) FR G01N-033-53
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IT LI LT LU
LV MC MK NL PL PT RO SE SI SK TR

ADT FR-----2853965 A1 2003FR-0050106 20030415; WO--2004092729 A2 2004WO-FR050158 20040413; EP-----1616185 A2 2004EP-0758930 20040413, 2004WO-FR50158 20040413

FDT EP-----1616185 A2 Based on WO--2004092729

PRAI 2003FR-0050106 20030415

IC ICM G01N-033-53; G01N-033-543
ICS C07B-061-00

AB FR 2853965 A UPAB: 20050126

NOVELTY - Method for screening the operating conditions for a coupling reaction between at least two functional groups.

DETAILED DESCRIPTION - Method for screening the operating conditions for a coupling reaction between at least two functional groups comprises:

(1) reacting at least two compounds, E1-X1-G1 and E2-X2-G2, in solution and under predetermined operating conditions, with at least one being a candidate operating condition (COC), to produce a compound (Z) of formula E1-X1-G1-G2-X2-E2;

(2) determining the concentration of (Z) at a predetermined time (t), by at least one immunological assay, using at least one antibody (AC1) specific for the molecule (M1) of which E1 is the residue; and

(3) evaluating the effect of one or more COC on the reaction, from the measured concentration of (Z).

G1, G2 = first and second functional groups;

X1 and X2 = covalent bonds or linkers;

E1 = residue of molecule M1 for which a specific antibody (AC1) is available;

E2 = residue of second molecule M2 for which a second antibody (AC2) is available, or a group able to form at least one covalent bond with AC1 in presence of a coupling agent

An INDEPENDENT CLAIM is also included for a kit for the new process.

USE - The method is used to select reaction conditions for optimization of yield and specificity in a wide range of coupling reactions, e.g. esterification; amidification; Heck, Michael, Diels-Alder, Suzuki or Mannich reactions, most especially selection of catalysts. These reactions are used in chemistry, agriculture, pharmaceuticals, and environmental protection; also in screening (a) libraries of enzyme mutants or (b) biological samples for presence of particular enzymatic activities.

ADVANTAGE - The method is suitable for high-throughput testing for reaction conditions, many of which can be tested simultaneously. It is compatible with all chemical or biological systems; does not require purification of reaction media; provides a quantitative assessment of the effects of reaction conditions; is very sensitive (Z can be detected at 10-9 M); is reproducible and simple (no special or expensive equipment is needed).

Dwg.0/3

FS CPI EPI

FA AB; DCN

MC CPI: B04-G21; **B04-L05**; B07-D09; B10-D01; B10-E02; B10-G02; B11-C01A; B11-C07A; B11-C08; B11-C10A; B12-K04E; **D05-A01**; **D05-A01B3**; D05-H09; E07-D09B; E10-A16A; E10-B01; E10-B02; E10-B02A3; E10-B03; E10-B04; E10-C02; E10-C03; E10-C04; E10-C04F; E10-D01D; E10-E01; E10-E02U; E10-E03; E10-G02H2; E10-J02C; E11-F06; **E11-F07A**; E11-M; J04-E01; N05-D
EPI: S03-E04E; S03-E09B; S03-E14H4

ABEX UPTX: 20050126

EXAMPLE - Compounds (V) and (VI) were prepared by condensing,

respectively, 6-nitrocaproic acid and histamine and N-(2-aminoethyl)-3-(4-formylphenyl)propionamide with homovanillic acid. They were then tested for coupling in two different solvents; in presence of 12 different catalysts and for 4 different times. The amounts of coupled product were determined by reaction with an anti-histamine antibody, immobilized on the wells of a microtiter plate and then by reaction with an anti-homovanillic acid antibody labeled with acetylcholine esterase (AchE). The amount of AchE bound was measured using acetylcholine idoide and Ellman's reagent, and measurement of absorption. A yield of over 50% coupled product, after 4 hours, was achieved (a) in tetrahydrofuran, with diazabicylo-octane or dimethylaminopyridine as catalyst, or (b) in dichloromethane with tetrabutylammonium fluoride as catalyst.

TECH UPTX: 20050126

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Materials: E1 and E2 are particularly haptens, especially one is the residue of histamine (optionally protected on the ring nitrogen) and the other is the residue of homovanillic acid (optionally protected on ring hydroxy). Other suitable include carboxy, formyl, aromatic hydroxy, alkenyl, azido or photo-activatable groups, but especially amino or thiol.

Preferred Process: The concentration of (Z) is determined by solid-phase immunoassay by reacting first with a solid phase that carries AC1, then reaction with labeled AC2. Alternatively where E2 can form covalent bonds with AC1, a coupling agent is used to form bonds between AC1 (immobilized) and E2 in immobilized (Z); immunological bonds present between AC1 and E2 are denatured so that the E2-component is released from the solid phase, then the solid phase is reacted with a conjugate of AC1 with a label so that the conjugate is immobilized by reaction with E1 of the (Z) released. The amount of conjugate fixed is then measured from the marker coupled to AC1. In both cases the concentration of (Z) is determined using a calibration curve. Antibodies are preferably monoclonal and supports are microtiter plate wells on which AC1 has been adsorbed. The preferred label is an enzyme, specifically acetylcholine esterase. The same method can be extended to reactions involving 3 or 4 functional groups, and then 2 or 3 immunological determinations are made. Specified COC are solvent, temperature, pressure, ultrasonic treatment, stoichiometric ratio, reaction time, but especially catalysts.

Preferred Kits: These contain E1-X1-G1 and E2-X2-G2; at least two antibodies; (Z) and optionally also reagents for measuring the marker, particularly an enzyme substrate, and buffers.

L62 ANSWER 2 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN **2003-815159** [77] WPIX
DNC C2003-227068
TI Preparation of enantiomerically enriched amino aldehyde or amino alcohol by subjecting enantiomerically enriched amino nitrile to hydrogenation in the presence of hydrogen, hydrogenation catalyst and mineral acid.
DC B05 D16 E19
IN BROXTERMAN, Q B; DASSEN, B H N; KAPTEIN, B
PA (STAM) DSM IP ASSETS BV; (BROX-I) BROXTERMAN Q B; (DASS-I) DASSEN B H N; (KAPT-I) KAPTEIN B
CYC 104
PI EP-----1352894 A1 20031015 (200377)* EN 8 C07C-213-08
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
WO--2003087033 A1 20031023 (200380) EN C07C-213-08
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU--2003224495 A1 20031027 (200436) C07C-213-08
EP-----1492760 A1 20050105 (200504) EN C07C-213-08
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

US--2005215822 A1 20050929 (200564) C07C-029-48
CN-----1646477 A 20050727 (200577) C07C-213-08
ADT EP-----1352894 A1 2002EP-0076383 20020409; WO--2003087033 A1 2003WO-NL000262 20030407; AU--2003224495 A1 2003AU-0224495 20030407; EP-----1492760 A1 2003EP-0721144 20030407, 2003WO-NL00262 20030407; US--2005215822 A1 2003WO-NL00262 20030407, 2004US-0510660 20041007; CN-----1646477 A 2003CN-0807986 20030407
FDT AU--2003224495 A1 Based on WO--2003087033; EP-----1492760 A1 Based on WO--2003087033
PRAI 2002EP-0076383 20020409
IC ICM C07C-029-48; C07C-213-08
ICS C07C-221-00
AB EP 1352894 A UPAB: 20031128
NOVELTY - Enantiomerically enriched amino aldehyde or amino alcohol is prepared by subjecting enantiomerically enriched amino nitrile to hydrogenation in the presence of hydrogen, hydrogenation catalyst and mineral acid.

DETAILED DESCRIPTION - Preparation of enantiomerically enriched compound of formula R1-C asterisk (R2)(NR4R5)-R3 (I) or its salt comprises subjecting enantiomerically enriched compound of formula (II) or its salt to hydrogenation in the presence of hydrogen, hydrogenation catalyst and mineral acid.

C asterisk = asymmetric C;
R1, R2, R5 = H or optionally substituted alkyl or aryl;
R3 = CH2OH or optionally protected CHO;
R4 = H, C(O)R6, or amine protecting group;
R6 = H or optionally substituted alkyl, aryl or alkoxy;
R4R5N = cyclic imide;
R7 = amine protecting group; and
R5R7N = cyclic amine.

USE - For preparing enantiomerically enriched compound.

ADVANTAGE - The nitriles (2) can easily and with good yield be converted into the corresponding compound (1) without racemization. Small amounts of diamines are formed as byproduct of the hydrogenation.

Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B07-H03; B10-A12C; B10-B03A; B10-B03B; B10-B04A; B10-B04B; **D05-A02**; D05-C; E07-H02; E10-A12C1; E10-B03A2; E10-B03B2; **E10-B04A1**; **E10-B04C1**; **E10-B04C2**; E11-J; E11-M
ABEX UPTX: 20031128
EXAMPLE - Concentrated hydrochloric acid (HCl) solution (2.2 equivalent) and Pd/carbon (Pd/C) were added to a solution of (R)-2-amino-2,3-dimethylbutyronitrile.HCl-salt (2.7 g) in methanol-water (1:1). The mixture was hydrogenated for 5 hours and 1 MPa of hydrogen pressure under vigorous stirring. Additional Pd/C (0.40 g) was added and the hydrogenation was continued for 23 hours at 5 MPa. The conversion to (R)-2-methylvalinol was greater than 90% and proceeded without racemization.

DEFINITIONS - Preferred Definition:
R3 = optionally protected CHO or CH2OH.
TECH UPTX: 20031128
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Condition: Hydrogen is present at a hydrogen-pressure of 0.1-2 (preferably 0.5-1) MPa. At least during part of the hydrogenation the hydrogen-pressure is 4-6 MPa. The hydrogen-pressure initially is 0.5-2 MPa and subsequently, after most of the nitrile starting material is converted, the hydrogen-pressure is increased to 2-10 MPa. Preferred Material: The palladium (Pd) catalyst is used as the hydrogenation catalyst. Preferred Method: The amino aldehyde is isolated in the form of a chemically and configurationally stable derivative. As starting material, an enantiomerically enriched nitrile is used that is prepared by (precursor) fermentation, enzymatic resolution, crystallization induced asymmetric transformation, classical resolution, resolution via preferential crystallization, diastereomeric synthesis,

catalytic asymmetric synthesis or dehydration of amino acid amides.

L62 ANSWER 3 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN **2003-106310** [10] WPIX
DNC C2003-027096
TI Enzyme activity inducers for asymmetric reduction of alpha-aminoketones for effective preparation of optically active beta-amino alcohols.
DC B05 D16 E19
PA (FUJY) FUJI PHARM IND CO LTD
CYC 1
PI JP--2002253224 A 20020910 (200310)* 16 C12N-009-00 <--
ADT JP--2002253224 A 2001JP-0058701 20010302
PRAI 2001JP-0058701 20010302
IC ICM **C12N-009-00**
ICS C12P-013-00
ICI C07M-007:00; C12R-001:80; C12R-001:665; C12R-001:66; C12R-001:65; C12R-001:645; C12R-001:34; C12R-001:32; C12R-001:22; C12R-001:01; C12P-013-00; C12P-013-00; C12P-013-00; C12P-013-00; C12P-013-00; C12P-013-00; C12P-013-00; C12P-013-00; C12P-013-00
AB JP2002253224 A UPAB: 20031006
NOVELTY - Enzyme activity inducers.
DETAILED DESCRIPTION - Enzyme activity inducers of formula (I) for asymmetric reduction of alpha-aminoketones, formula (1), used for preparation of optically active beta -aminoalcohols of formula (3) by culture of a microorganism in the presence of alpha -aminoketones or their enantiomers of formula (2), formula (2), formula (3). Also claimed microorganisms used for the reaction.
A = R4-CO- (Y) or R5-O-C(R6)(R7)- (Z);
R4, R6 = H atom, an optionally substituted 1-3C alkyl group;
R4+R8 = a 5-10C hydrocarbon ring or a 5-8 membered heterocyclic skeleton containing 1-3 heteroatom(s);
R5 = H atom, a 1-3C alkyl group;
R5+R6, R5+R9 or R6+R9 = a 5-8 membered heterocyclic skeleton containing 1-3 heteroatom(s);
R6+R8 = a 5-10C hydrocarbon ring;
R7, R10 = H atom, an optionally substituted 1-6C alkyl group;
R8 = H atom, carboxyl, an optionally substituted 1-6C alkyl group;
R9 = H atom, an optionally substituted (1-6C (alkyl or alkyloxycarbonyl) or acyl) group;
X = a halogen atom, a lower alkyl group, an optionally protected OH , nitro, or sulfonyl group(s);
n = 0, 1, 2 or 3; and
asterisk = an asymmetric carbon atom.
USE - Induction of enzyme activity for asymmetric reduction of alpha-aminoketones
ADVANTAGE - Highly selective and high yield preparation of beta -aminoalcohols.
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B04-F09; B04-F10; B07-H01; B07-H02; B10-A10; B10-A12C; B10-B02H; B10-B02J; B10-B03B; B10-B04B; B10-C04D; B10-D01; B10-D03; D05-C; D05-H04; D05-H05; D05-H08; E07-H01; E07-H02; E10-A10C; E10-A12C1; E10-B02D4; E10-B02D7; E10-B02D8; E10-B03B; **E10-B04C**; E10-C04D1; E10-C04D3; E10-C04D5; E10-D01C; E10-D03C; E10-D03D; E11-D; E11-M
ABEX UPTX: 20031006
SPECIFIC MICROORGANISMS - 30 species of microorganisms are disclosed in claims including Rhodococcus erythropolis MAK-34 (FERM BP-7451).

EXAMPLE - In a culture medium, 1-amino-2-hydroxypropane (5 g/L, 5 ml) was added and sterilized at 121 degrees C for 30 minutes. Then, Rhodococcus erythropolis MAK-34 (FERM BP-7451) was inoculated and cultured at 30 degrees C and 300 rpm for 48 hours. The cultured mixture (0.5 ml) was centrifuged at 10,000G for 20 minutes to give cultured cells. The cells were suspended in water, a buffer and dl-2-methylaminopropiophenone HCl

(10 mg) to make reaction mixture (1 ml) and incubated at 30 degrees C and 150 rpm for 12 hours. The reaction mixture was centrifuged to give pseudoephedrine solution with improved formation in comparison to a similar reaction carried out without addition of microorganisms.

L62 ANSWER 4 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN **2002-519068** [55] WPIX
DNC C2002-146744
TI Preparation of enantiomerically enriched acylated amine involves contacting enantiomerically enriched compound with mixture of enantiomers of corresponding amine in the presence of Pen-G acylase.
DC B04 D16 E16
IN GURANDA, D T; KHIMIOUK, A I; SHELDON, R A; SVEDAS, V K; VAN LANGEN, L M; VAN RANTWIJK, F
PA (STAM) DSM NV
CYC 97
PI WO---200220821 A2 20020314 (200255)* EN 12 C12P-041-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU---200194378 A 20020322 (200255)
AU--2001294378 A8 20050908 (200568) C12P-041-00
ADT WO---200220821 A2 2001WO-NL000643 20010831; AU---200194378 A 2001AU-0094378 20010831; AU--2001294378 A8 2001AU-0294378 20010831
FDT AU---200194378 A Based on WO---200220821; AU--2001294378 A8 Based on WO---200220821
PRAI 2000NL-1016127 20000908
IC ICM C12P-041-00
ICS C07C-237-06; C12P-013-00; C12P-013-02
AB WO 200220821 A UPAB: 20020829
NOVELTY - Enantiomerically enriched acylated amine (I) is prepared by contacting an enantiomerically enriched compound (II) with a mixture of enantiomers of a corresponding amine (III) in the presence of a Pen-G acylase.

DETAILED DESCRIPTION - Preparation of an enantiomerically enriched acylated amine of formula (I), comprises contacting an enantiomerically enriched compound of formula (II) with a mixture of enantiomers of a corresponding amine of formula (III) in the presence of a Pen-G acylase.

R1, R2, R3 = H, CN, (un)substituted (cyclo)alkyl, aryl alkylaryl or arylalkyl, cyclic or non-cyclic heteroalkyl or heteroaryl with one or more N, O or S atoms or (CH2)n-COR4;

n = 0-6;

R4 = OH or (un)substituted alkyl, aryl, alkoxy or amino;

X = NH2, OH, halo, alkoxy, or alkyl;

R5 = Ph (that can be substituted with substituents from halo, OH, nitro, alkoxy or alkyl);

Z = NH2, NH-OH, NH-NH2, NH-R6;

R6 = 1-6C alkyl

USE - For preparing an enantiomerically enriched acylated amine (claimed).

ADVANTAGE - The process givess enantioselectively acylate amines with a higher enantioselectivity and a higher yield. The reaction proceeds more rapidly or less enzyme is needed and/or a higher yield is obtained compared with reactions where phenylacetic acid is used as an acylating agent. When the enantiomerically enriched compound is used, a higher S/H ratio (ratio of synthesis of acylated product to hydrolysis of the enantiomerically enriched compound) is achieved in the acylation.

Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: **B04-L04B**; **D05-A02**; E06-H; E07-H; E10-A15E; E10-B02A3; **E10-B04C1**; E10-D03C3
ABEX UPTX: 20020829

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EXAMPLE - (R, S)-2-amino-4-phenylbutane (0.17 g) and (R)-phenylglycine amide (0.23 g) were added to water (5 ml). Subsequently, the pH was brought to 10 with 3N hydrochloric acid. The reaction mixture was subsequently stirred for 5 minutes with its temperature brought to 25degreesC. Subsequently, an aqueous solution (0.08 ml) of A. faecalis (2.3x10-4 M, 1060 U/ml) was added. During the enzymatic acylation, the pH was kept at 10 with a 2M potassium hydroxide solution. After 25 minutes, 50% acylation was achieved. The precipitated product was filtered off and washed with 2 x 2 ml water and dried to constant weight. The analysis showed that the product had a yield of 0.16 g of N-phenylglycine-(R)-2-amino-4-phenylbutane with an enantiomeric excess (ee) of greater than 99% and a stereospecificity (E) of greater than 200.

TECH UPTX: 20020829

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The enantiomerically enriched enantiomer of the compound or at least one of the enantiomers of the compound of formula (II) is applied. The enantiomerically enriched acylated amine is subsequently contacted with the Pen-G acylase which is derived from Alcaligenes faecalis. The pH is 4-8. The non-acylated enantiomer of the amine is isolated from the acylated amine.

Preferred Property: (I) has a diastereomeric excess of greater than 90 (preferably greater than 98)%.

L62 ANSWER 5 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2002-454722 [48] WPIX
DNC C2002-129343
TI Use of mutated enzymes for chemically transforming compounds e.g. amine from ketone.
DC B05 D16 E19
IN **ROZZELL, J D**
PA (ROZZ-I) ROZZELL J D; (BIOC-N) **BIOCATALYTICS INC**
CYC 98
PI WO---200236742 A2 20020510 (200248)* EN 28 C12N-000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US--2002061564 A1 20020523 (200248) C12P-013-04 <--
AU---200232603 A 20020515 (200258)
AU--2002232603 A8 20051013 (200611) C12P-013-04
ADT WO---200236742 A2 2001WO-US048577 20011030; US--2002061564 A1 CIP of **2000US-0702421 20001031, Provisional 2001US-288378P 20010503 , 2001US-0039952 20011024**; AU---200232603 A 2002AU-0032603 20011030; AU--2002232603 A8 2002AU-0232603 20011030
FDT AU---200232603 A Based on WO---200236742; AU--2002232603 A8 Based on WO---200236742
PRAI **2001US-0039952 20011024; 2000US-0702421 20001031; 2001US-288378P 20010503**
IC ICM C12N-000-00; C12P-013-04
ICS C12P-013-06; C12P-013-22; C12Q-001-32; C12Q-001-52
AB WO 200236742 A UPAB: 20020730
NOVELTY - Production of an amino acid, amine or an alcohol from a target (2-ketoacid (for amino acid) or ketone (for amine and alcohol)) involves creating a mutated enzyme that catalyzes the reductive amination or transamination of the target compounds or reduces the target ketone (for the production of alcohol) to form the respective products.

USE - For the production of amino acids (preferably chiral), alcohols or amines (claimed) and for producing chiral intermediates useful in pharmaceutical and agricultural industries.

ADVANTAGE - The mutated enzyme catalyzes the reductive amination or transamination of the target compounds or reduces the target ketone (in the production of the alcohol) at a greater rate than the existing enzyme. By determining in which reaction the pH indicator undergoes a color change the enzymatic activities can be detected easily even in a high throughput

format enabling more facile discovery of new enzymes, particularly oxidoreductases that catalyze useful redox reactions. The enzymes are easier to use and are more cost effective than performing an asymmetric synthesis and can perform chemical transformations exclusively forming one enantiomeric product.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-L03D; B04-L04; B10-B02; B10-B04; B10-E04; B11-A02; D05-A02; E05-G03C; E10-B02D2; E10-B02D6; E10-B04C1
ABEX UPTX: 20020730
EXAMPLE - Amine dehydrogenase (100 units) generated by mutagenesis and screening of leucine dehydrogenase was incubated at 45degreesC in a solution (100 ml) maintained at pH 6.5 containing potassium phosphate (1 mmole), nicotinamide adenine dinucleotide (NADH) (0.01 mmole), ammonium formate (25 mmole) and formate dehydrogenase from Candida boidinii (100 units). Acetophenone (10 millimoles) was added slowly over one hour with stirring and the reaction was allowed to proceed for an additional 4 hours. After basification of the reaction mixture to pH 12 and extraction with methyl tert-butyl ether, analysis of the reaction products was carried out by gas chromatography to yield 1-phenylethylamine.
TECH UPTX: 20020730
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: The process further involves providing an existing enzyme that catalyzes the reductive amination or transamination of the target compounds or reduces the target ketone (for the production of alcohol) and creating the mutated enzyme by mutating the existing enzyme. The reaction mixture for the production of the amino acids further comprises recycled nicotinamide cofactor.
Preferred Components: The target 2-ketoacid is 3,3-dimethyl-2-ketobutyrate, 3-(2-naphthyl)pyruvate, 3-(1-naphthyl)pyruvate or 4-(methylphosphinyl)-2-ketobutyrate.
TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The production of the mutated enzyme involves:
(a) mutating an existing enzyme to produce the mutated enzyme;
(b) determining the activity of the mutated enzyme on the target compounds by contacting the mutated enzyme with a composition comprising the target compounds and pH indicator and determining the change in the pH of the composition using the pH indicator; and
(c) determining whether the mutated enzyme catalyzes the reductive amination or transamination of the target compounds or reduces the target ketone (for the production of alcohol) at a greater rate than the existing enzyme.
Step (b) involves detecting an optical change in the composition.
Preferred Components: The mutated enzyme for the reductive amination in the production of the amino acid or amine is an amino acid dehydrogenase (preferably leucine dehydrogenase or phenylalanine dehydrogenase). The mutated enzyme for the transamination in production of the amino acid or amine is aspartic-glutamic transaminase, aromatic amino acid transaminase or branched-chain amino acid transaminase. The mutated enzyme for the formation of alcohol is alcohol dehydrogenase, ketoreductase or carbonyl reductase (preferably alcohol dehydrogenase YPR1).

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - The reaction mixture for the production of amino acids further comprises ammonia or its salt.

L62 ANSWER 6 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN **1988-268207** [38] WPIX
DNC C1988-119514
TI Organic halo cpds. such as p-bromo anisole, preparation - involves halogenation in non-haem type bromo peroxidase, peroxide and halide.
DC D16 E19
PA (AMAN) AMANO PHARM KK
CYC 1
PI JP----63196295 A 19880815 (198838)* 6
ADT JP----63196295 A 1987JP-0030236 19870212
PRAI 1987JP-0030236 19870212

noble jarrell 19/10/2006

IC C12P-005-00; C12P-007-00; C12P-009-00
AB JP 63196295 A UPAB: 19930923
An organic cpd. is halogenated in the presence of a non-haem type bromoperoxidase, a peroxide and a halide ion.

The non-haem type bromoperoxidase for use in the process is obtd. from Corallina marine algae, such as Corallina officinalis, Corallina pilulifera, Corallina squamata, Serraticardia maxima, Calliarthron yessoense, etc. Organic cpds. to be halogenated as substrate for the enzyme are beta-diketones R-CO-CH2-CO-R, phenol derivs. (I), aniline derivs. (II) substd. alkene derivs. R-CH=CH-R (III).

In the formulae, R is H, alk(en)yl, phosphoric acid, or alk(en)yl substd. by one or more substits. selected from OH, alkoxy, amino, nitro and halo, or (un)substd. alicyclic hydrocarbon, or (un)substd. phenyl or benzyl.

ADVANTAGE - The halogenation may be conducted under a mild condition.

0/0
FS CPI
FA AB; DCN
MC CPI: **D05-A02A**; D05-C03B; E05-G08; E05-G09A; E05-G09D; E10-B01A; E10-B03; E10-B04A; **E10-B04C**; E10-D01C; E10-E02B; E10-E02C; E10-E04C; E10-E04F; **E10-F02**; E10-G03; E10-H01D; E10-H01E; E10-H02

=> d his

(FILE 'HOME' ENTERED AT 14:59:08 ON 19 OCT 2006)

FILE 'HCAPLUS' ENTERED AT 15:01:36 ON 19 OCT 2006
L1 1 US2002061564/PN OR (US2001-039952 OR US2000-702421 OR US2001-28
E ROZZELL J/AU
L2 79 E3-8
E ROZZELL D/AU
L3 10 E4-5
L4 45 BIOCATALYT?/CS,PA

FILE 'REGISTRY' ENTERED AT 15:03:52 ON 19 OCT 2006

FILE 'HCAPLUS' ENTERED AT 15:03:52 ON 19 OCT 2006
L5 TRA L1 1- RN : 43 TERMS

FILE 'REGISTRY' ENTERED AT 15:03:53 ON 19 OCT 2006
L6 43 SEA L5
L7 STR
L8 50 L7
L9 SCR 1087 OR 1151 OR 1152 OR 1139 OR 1140
L10 50 L7 AND L9
L11 STR
L12 41 L11
L13 9467 L11 FULL
SAV TEM L13 GIT952N/A

FILE 'HCAPLUS' ENTERED AT 15:08:03 ON 19 OCT 2006
E KETONES/CT
E E3+ALL
L14 QUE E4+NT
L15 177969 L14 (L) RACT+NT/RL
L16 8511 L13 (L)RACT+NT/RL
L17 172148 L15 NOT L16
L18 9 L17 AND L1-4
E AMINATION/CT
E E3+ALL
L19 13961 E2+NT OR E11+OLD,NT OR E12+OLD,NT
L20 1 L18 AND L19
E AMINES/CT
L21 72725 E3+OLD,NT1 (L) PREP+NT/RL

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                E AMINES, PREP/CT
L22         41176 E4-7
L23         13279 AMINE#/CW (L)PREP+NT/RL
L24          7013 L17 AND L21-23
L25           467 L24 AND L19
                E ENZYMES/CT
L26             QUE E3+OLD,NT1 OR ENZYME#/CW
L27               4 L25 AND L26
L28               4 L20,L27

     FILE 'WPIX' ENTERED AT 15:21:39 ON 19 OCT 2006
L29              50 L7
L30              36 L11
L31             509 L11 FULL
                SAV TEM GIT952N2/A L31
L32          354340 E10-F?/MC OR J5?/M0,M1,M2,M3,M4,M5,M6
L33           12571 C07C049/IPC,IC,ICM,ICS,ICA,ICI
L34             943 L31/DCR
                DEL SEL Y
                SEL SDCN L31
                EDIT /SDCN /DCN
L35            1571 E1-515
                DEL SEL Y
                SEL DCSE L31
                EDIT /DCSE /DCRE
L36             943 E1-509
                DEL SEL Y
                SEL SDRN L31
                EDIT /SDRN /DRN
L37            1162 E1
L38          354905 L32-33 NOT L35-37
L39             164 L38 AND E11-F07A/MC
L40              39 L39 AND (E10-B01A3 OR E10-B04A1 OR E10-B04C?)/MC
L41             148 L39 AND (H1? OR H2?)/M0,M1,M2,M3,M4,M5,M6
L42              26 L39 AND C07C209/IPC,IC,ICM,ICS,ICA,ICI
L43             148 L40-42
L44               0 L43 AND V8?/M0,M1,M2,M3,M4,M5,M6
L45               3 L43 AND (B04-L? OR C04-L? OR B04-B02C? OR C04-B02C?  OR D05-A?)
L46               1 L43 AND (C12N009 OR C12Q)/IPC,IC,ICM,ICA,ICI,ICS
L47             691 L38 AND (E10-B01A3 OR E10-B04A1 OR E10-B04C?)/MC
L48          248325 L38 AND (H1? OR H2?)/M0,M1,M2,M3,M4,M5,M6
L49             689 L38 AND C07C209/IPC,IC,ICM,ICS,ICA,ICI
L50              11 L47 AND (V8?/M0,M1,M2,M3,M4,M5,M6 OR (B04-L? OR C04-L? OR B04-B
L51              14 L45-46,L50
                SEL AN 3 5 7 10 13
L52               5 L51 AND E2-6
L53               1 L1
                E ROZZELL J/AU
L54              21 E3-4
L55               7 E1-2
L56              18 BIOCATALYTIC?/CS,PA
                E BIOC/PACO
                E E3+ALL
L57             188 E1
L58               0 L39 AND L53-57
L59             115 L32-33 AND L53-57
L60               0 L59 AND E11-F07A/MC
L61               1 L34-37 AND L53-57
L62               6 L52,L61

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